

Applicants submit that the proposed amendments of claims 6-9 do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Rejections under § 112, second paragraph

Claims 6 and 7 have been rejected under 35 USC § 112, second paragraph as unclear as to what is considered a "suitable" signal peptide. Applicants assume the Examiner is referring to claim 8, not claim 7. For the reasons described in the Amendment and Response of October 10, 2002, Applicants respectfully traverse. However, in an effort to expedite prosecution, Applicants have amended the claims to remove the term suitable. The scope of the claims is unchanged by this amendment. Applicants respectfully request that this rejection be withdrawn.

Rejections under § 112, first paragraph

Claims 6-8 remain rejected under 35 USC § 112, first paragraph because the specification does not reasonably provide enablement for a process for selecting a suitable signal peptide for secretory expression of any desired protein using the method steps of the claims. For the reasons described in the Amendment and Response of October 10, 2002, Applicants respectfully traverse.

In the Official Action, the Examiner again admits that the instant application is enabling for a process for selecting a suitable signal peptide for secretory expression of hirudin or a hirudin derivative using the method steps of the claims. Thus, in an effort to expedite prosecution, Applicants have amended the claims to recite a

process for selecting a signal peptide for secretory expression of a desired hirudin or hirudin derivative protein in *E. coli*. Applicants respectfully request that this rejection be withdrawn.

Rejections under § 103

Claims 6, 7, and 9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Achstetter et al. in view of Schmid et al. Applicants respectfully traverse.

Applicants again point out that there would be no motivation to use the yeast signal peptides of Aschtetter et al. in the specific system of Schmid et al., which is optimized for *E. coli* signal peptides. The Examiner responded to this argument by stating that the claims are not limited to the type of signal peptides that are used in the method, therefore the rejection is maintained. Applicants respectfully believe that the Examiner is missing the point of Applicants' argument.

Applicants' claims and disclosure is irrelevant in the determination of a teaching or suggestion to make the claimed combination when the Examiner is establishing a *prima facie* case of obviousness. See M.P.E.P. § 706.02(j). Motivation can only be determined from the nature of the problem to be solved, the teachings of the prior art, and the knowledge of a person of ordinary skill in the art. See M.P.E.P. § 2143.01.

The requisite motivation is lacking in the prior art. Achstetter et al. only uses yeast signal peptides. Schmid et al. teaches special *E. coli* strains that are mutants specifically chosen to provide optimum secretion with signal peptides known to allow permeation of the membrane of *E. coli* cells. Simply put, there would be no

motivation to use yeast signal peptides in a specific system which is optimized for *E.coli* signal peptides.

As explained in the response of October 10, 2002, the references must be read as a whole, including portions that teach away from the proposed modification. See e.g., M.P.E.P. § 2143.01. The Examiner's argument is based on his assessment that the Schmid et al. achieves the goal of improving *E. coli* expression. See Official Action, page 11. However, this goal is only achieved using a special *E. coli* mutants with special *E. coli* signal peptides. Schmid et al, col 3, line 32, to col. 4, line 11. The Examiner ignores that in addition to the passages quoted by her, Schmid also states that the yield in *E. coli* is **relatively low** and the isolation processes are **complicated**.

Thus, Applicants maintain that there would be no motivation to use the yeast signal peptides of Aschtetter et al. in the specific system of Schmid et al., which is optimized for *E.coli* signal peptides, and respectfully request that this rejection be withdrawn.

Conclusion

Finally, applicants submit that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

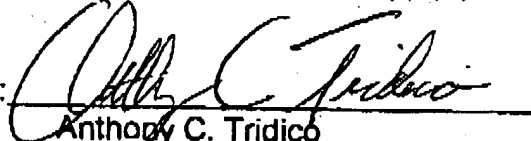
Please grant any extensions of time required to enter this response and
charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: April 7, 2003

By:


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